Remarks:

Claims 1-61 are pending in this application. Claims 22, 24, 27, 28, 29, 30, 31, 47, 48, 49, 51, 52, 54, 55, 56 and 61 have been amended.

Claims 1-21, 23, 25, 26, 32-46, and 50 are withdrawn. Examiner's reconsideration of withdrawn claims and indication that previously withdrawn claims 28-31, 49, 51, 52, 54, 58, 59 and 60 are appropriate for continued examination in the present application is gratefully acknowledged.

Claim Objections

The objection to claims 28-31 and 54 under 37 CFR 1.75(c) is *moot*, as claims 28-31 are now each singly dependent, and claim 54 has been amended to clarify that its multiple dependency is in the alternative.

Claims 22 and 28-31 are amended to overcome any rejection under 35 USC 101 and 112.

Claim Rejections Under 35 USC § 112

Claims 47, 51, 55 and 57-60 are rejected under 35 USC § 112, first paragraph, for failing to comply with the written description requirement.

The following guidance is provided at page 6, paragraph 3 of the Office Action:

> "While the skilled artisan may be readily able to prepare nucleic acid constructs and more specifically siRNA constructs which can target cytokines, the claims are broadly drawn to any construct that targets any cytokine, known or yet to be discovered, produced by an antigen presenting cell."

The above quoted guidance is interpreted to indicate that a further definition of "construct" to specify "nucleic acid" or "siRNA" would overcome the rejection.

For the purpose of advancing prosecution and without acceding to Examiner's rejection, independent claims 47, 51 and 55 have been amended to replace each occurrence of "construct" with "siRNA", and dependent claims 57-60 incorporate the recitation of "siRNA" by virtue of dependency. Therefore, in view of the above quoted guidance, the rejection of claims 47, 51, 55 and 57-60 under 35 USC § 112, first paragraph is believed to be *moot*, and withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 USC §102

Claims 55 and 57-60 are rejected under 35 USC § 102(b) as being anticipated by Kato *et al*. Claims 47, 48, 49, 51, 52, 53, and 55-61 are rejected under 35 USC § 102(e) as being anticipated by Qian *et al* as evidenced by Li *et al*.

Examiner will kindly note that each of the rejected claims either explicitly recite "siRNA" or incorporate this recitation by virtue of dependency.

None of the cited references teach or suggest siRNA.

Qian *et al* suggest the use of "antisense technology, intrabodies, ribozymes, gene silencing techniques, and the like." However, no mention of siRNA can be found throughout the Qian *et al* reference.

At page 9, paragraph 2 of the Office Action, Examiner asserts that gene silencing methods encompass siRNA.

Applicants submit that gene silencing methods encompass many techniques including transposon silencing or transgene silencing, both of which were well established at the filing date of the Qian *et al* reference. Thus, a suggestion of gene silencing is not equivalent to a suggestion of siRNA.

As such, the cited references do not teach each and every element recited in the present claims.

For at least these reasons, claims 55 and 57-60 are submitted to be compliant with 35 USC § 102(b) and claims 47, 48, 49, 51, 52, 53, and 55-61 are submitted to be compliant with 35 USC § 102(e), and withdrawal of each rejection is respectfully requested.

Claim Rejections Under 35 USC § 103

Claims 22, 24, 27, 47, 48, 49, 51, 52, 53 and 55-61 are rejected under 35 USC § 103(a) as being unpatentable over the combination of Robbins *et al*, Li *et al*, Hammond *et al* and Tuschl *et al*.

Robbins *et al* describe the use of an oligonucleotide that contains at least one binding site for the NF-kB transcription factor. The oligonucleotide acts as a decoy to inhibit binding of NF-kB to its endogenous targets and thus generally interferes with NF-kB-dependent transcription (see for example, column 6, lines 17-23).

The oligonucleotide approach of Robbins *et al* is entirely unrelated to siRNA as recited in the present claims. The oligonucleotide of Robbins *et al* physically binds with a protein NF-kB, while an siRNA targets expression of a gene based on sequence

homology. The oligonucleotide of Robbins *et al* is a generalized approach that interferes with transcription of all NF-kB-dependent transcription, while an siRNA can target production of a specific molecule.

The skilled person having read Robbins *et al* would have no reason to expect that the generalized interference of NF-kB-dependent transcription could be replaced with a targeted interference of a specific molecule provided by siRNA. Indeed, the skilled person would expect that the generalized interference of NF-kB-dependent transcription taught by Robbins *et al* is crucial to achieve the resulting tolerogenic dendritic cells and their associated benefits.

Li *et al* describe an antibody that interacts with IL-12, and correlate increased antibody dosing with prolonged graft survival. The skilled person would not combine the generalized transcriptional interference of Robbins *et al* with the specific antibody mediated antagonism of secreted IL-12 taught by Li *et al*. The difference between the general approach and the specific approach is too great to allow a proper combination. Moreover, the combination does not provide each and every claimed element. Using the teachings and techniques of Robbins et al., and Li et al., would not provide any success at achieving the presently claimed invention since the technical approaches are different to that claimed.

However, even if combined, the teachings of Robbins *et al* and Li *et al* would not lead the skilled person to a successful targeted interference of production of a specific molecule in an antigen presenting cell as provided by the present claims. The antibody of Li *et al* is designed to interact with IL-12 that has been produced and secreted by antigen presenting cells. Accordingly, the teachings of Li *et al* are limited to the post-translational antagonism of secreted IL-12. Li *et al* provide no teaching or suggestion that the effect of graft survival could be replicated with interference of the transcription or translation of the IL-12 molecule within an antigen presenting cell. Thus, the skilled person having read both Robbins *et al* and Li *et al* would have no expectation of success of achieving tolerogenic dendritic cells using a targeted interference of the transcription or translation of a specific molecule within such cells.

Hammond *et al* and Tuschl *et al* are focused on RNA interference technology and provide no teachings of suppressing T cell activity by targeting a specific molecule produced within an antigen presenting cell. Therefore, Hammond *et al* and Tuschl *et al* provide no teaching or suggestion to remedy the deficiencies of Robbins *et al* and Li *et al*.

In addition, Examiner will kindly note that the field of siRNA was not at the level it is today at the time the claimed invention was made. Indeed, Hammond *et al* do not even mention the term "siRNA." Furthermore, Hammond *et al* describe the use of RNA interference in *C. elegans*, *Drosophila*, Trypanosomes and plants (see page 116, Box 3), none of which possess an adaptive immune system with T cells and antigen presenting cells. Tuschl *et al*, published a mere four days in advance of the priority date of the present application, only provide evidence using Drosophila lysates and HeLa cell tissue cultures, none of which pertain to an adaptive immune system with T cells and antigen presenting cells.

Accordingly, the presently claimed invention is submitted to be patentable over Robbins *et al*, Li *et al*, Hammond *et al* and Tuschl *et al*, either alone or in combination.

For at least these reasons, claims 22, 24, 27, 47, 48, 49, 51, 52, 53 and 55-61 are submitted to be compliant with 35 USC § 103(a), and withdrawal of this rejection is respectfully requested.

Conclusion

For the reasons detailed above, it is submitted all remaining claims (Claims 22, 24, 27, 47-49, 51-53 and 55-61) are now in condition for allowance. An early notice to that effect is therefore earnestly solicited.

☒ This is an authorization under 37 CFR 1.136(a)(3) to treat any concurrent or future reply, requiring a petition for extension of time, as incorporating a petition for the appropriate extension of time.

☒ The Commissioner is hereby authorized to charge any filing or prosecution fees which may be required, under 37 CFR 1.16, 1.17, and 1.21 (but not 1.18), or to credit any overpayment, to Deposit Account 192253.

In the event the Examiner considers personal contact advantageous to the disposition of this case, he/she is hereby authorized to call Dr. Lola A. Bartoszewicz, at Telephone Number (416) 849-8420.

Respectfully submitted,

SIM & MCBURNEY

April 16, 2009
Date

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